

AMENDMENT

In the Specification:

At page 1, lines 6-9 of the specification, after the title, please delete the existing paragraph and replace with the following paragraph, so that the text reads:

The present application is a nationalization of PCT Application Serial No. PCT/US00/15243, filed June 02, 2000, which claims priority to United States provisional application Serial No. 60/137,470, filed June 04, 1999. The government owns rights in the present invention pursuant to grant number from R37-AG-10488, ROI-DK-14744, and NIH Training Grant T32 AG-AG-DO165, the National Institutes of Health.

At page 3, lines 14-21 of the specification, the final text is as follows:

At page 3, lines 14-21 of the specification, please delete the existing paragraph and replace with the following paragraph, so that the text reads:

The exemplary ribozymes, designated RZ-1 through RZ-7, cleave the human ER α mRNA at specific nucleotide positions (+377, +889, +894, +956, +1240, +1420, +1680, +1695, +1726 and +2077). They have a characteristic critical region defined by their nucleotide sequences. Even minor substitution at this region may result in significant loss of binding activity. The cleavage sites lie within the coding sequence for the DNA-binding domain of the receptor protein. The ribozyme constructs are also effective in inhibiting the progression of quiescent MCF-7 breast cancer cells to the S phase of the cell cycle after their exposure to 17 β -estradiol (10⁻⁹M).

At page 4, lines 26-33 of the specification, please delete the existing paragraph and replace with the following paragraph, so that the text reads:

The hammerhead ribozymes described here, selectively inhibit estrogen action by cleaving the hER α mRNA within its DNA-binding domain. The specifier side arms of both RZ-1 and RZ-2 do not show any significant homology to any known human mRNA species, except three related receptors, hERR-1, hERR-2, and hER β . RZ-2 possesses a slightly greater homology with hER β (90% sequence homology with respect to both side arms) than RZ 1 (one side arm, 90%; the other, 70%). RZ-2 provides a slightly better inhibitory function on the activity of the ERE-TK-Luc plasmid in transfected MCF-7 cells than the RZ1.

At page 22, lines 27-31 of the specification, please delete the existing paragraph and replace with the following paragraph, so that the text reads:

Positions of other GUC (GUC in RNA and GTC in corresponding cDNA) sequences are 170, 190, 267, 377, 508, 515, 543, 603, 645, 889 (cleavage site within the human mRNA for estrogen receptor for RZ-2), 894, 956 (cleavage site for RZ-1), 1137, 1218, 1240, 1420, 1463, 1468, 1680, 1695, 1726, and 2077. Sites # 889 and 956 were chosen because they met two other requirements, which are:

In the Claims:

After entry into the U.S. national stage, and assurance of a U.S. filing date, please revise the claims from the PCT application as follows.

Please cancel claims 1-22, without prejudice and without disclaimer.

Please add new claims 23-50, as follows:

23. (New) A ribozyme that cleaves estrogen receptor mRNA, wherein said ribozyme comprises the sequence of SEQ ID NO:7 (RZ1) or SEQ ID NO:11 (RZ2).